Participant Assessment for All Experiments

For participant assessment, psychiatric diagnoses were made by master's- or doctoral-level clinicians trained to reliability (κ>0.9) using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (KSADS-PL) and confirmed with a senior psychiatrist. Patients met full DSM 5 criteria for lifetime DMDD. Patients had abnormal irritable or angry mood and developmentally inappropriate outbursts at least 3 times per week. DMDD symptoms must begin before age 10, occur for ≥1 year without remission exceeding three months, and cause functional impairment in 2 settings. Patients with a history of euphoric mood or distinct (hypo)manic episodes lasting >1 day, or 6-month history of major depressive disorder, post-traumatic stress disorder, conduct disorder, psychosis, or autism spectrum disorder were excluded. Healthy volunteers were free of any KSADS-PL diagnoses. Exclusion criteria for all participants were chronic or active medical condition, psychoactive substance use within last 2 months, history of head trauma, current psychotropic medication use, and FSIQ < 70. Intelligence was measured using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler 1998).

Determining the 70% Accuracy Threshold for Experiment 1

Task disengagement, which is common amongst youths with DMDD and adds substantial noise to analyses, may lead to false negatives, or Type II error. To reduce Type II error, we set an accuracy threshold for excluding individuals making random to near-random responses. We selected the four most overtly angry and happy faces of the Interpretation Bias Task (IBT) from each of the four face-identities. Given each face was presented 3 times, there were a total of 48 unambiguous trials. We used accuracy on these unambiguous faces as a proxy measure of task engagement. In general, accuracy was very high (median accuracy=90%) for judgments of these unambiguous faces (Supplemental Figure 1). Inconsistent, near random judgments were evident in plots of responses by individuals whose accuracy was below 70%; their mean accuracy was 59%. We set the threshold at 70%, rather than at a higher point, because a higher threshold might exclude individuals with face-emotion labeling impairment indicative of DMDD. Therefore, we favored the risk of Type II error over reduced generalizability of our results to other samples of youth with DMDD.

Modeling Balance Point

Our parameter of interest is the morph at which judgments switch from happy to angry. One of the most established methods to predict a person's categorical judgment of items that differ along a continuum is to model the probability to making one judgment over another with a logistic curve (Luce 1959**;** Rasch 1980). Consistent with this prior work, Pollak & Kistler (2002) used a logistic curve to model the probability of making one face-emotion judgment over another on a continuum of morphs between two face-emotions. In Experiment 1, we used a 4-parameter logistic curve given by the following equation:

$$f(x) = c + \frac{d - c}{1 + \exp(bx - e)}$$

The inflection point (*e*) is halfway between the maximum probabilities of making angry or happy judgments, which we take as the balance point at the group level.

The package *drc* in R has the capability of fitting and comparing logistic curves among multiple groups using raw observations. Because there is no data reduction, this single-step approach is often statistically more powerful than a two-stage analysis where balance point is first estimated at the individual level and then analyzed at the group level. Preserving observations reduces the error, i.e. increases the precision, of the group-level balance point estimate. For example, in Experiment 1, all 180 responses made by all participants were directly entered into the estimate of two group-level curve fits, and the two curves were compared in a single model. In Experiment 1, the group-level logistic curves fit the data very well ($\chi^2(1323) = 2180$, $p<0.001$, main text Figure 2) and we did not detect any high leverage or outlying values (Cook's *D*'s ≤ 0.0002).

At times, it may be necessary to calculate individual-level balance points as in Experiments 2 and 3. To do so, one may either use a logistic curve fit or simple proportion (Pollak & Kistler, 2002; Penton-Voak et al., 2013), with the latter method being more feasible to implement in a software environment that does not have nonlinear curve-fitting support. To test the similarity of proportional and logistic curve based balance point estimates, we computed both for 55 of the 56 pre-training assessments of the tIBT task in Experiment 3. A logistic curve did not fit data from one subject. Balance point estimated by the proportion or inflection point methods were highly correlated ($r(53)=0.78$) and had similar means (*t* test $p=0.96$) and variances (Levene's test $p=0.86$); mean (*SD*) proportional and logistic curve based balance point estimates were 8.60 (1.91) and 8.58 (1.52), respectively.

Scan Acquisition

Magnetic resonance images were acquired on a General Electric 3.0 Tesla scanner with a 32 channel head coil. Blood oxygen-level dependent (BOLD) signal was measured by echoplanar imaging (EPI) the following parameters: flip angle=50º, echo time=25ms, repetition time=2.3s, 182 volumes per run, 3 runs, field of view=240mm, and acquisition voxel size=2.5x2.5x3mm. Total acquisition time was 21 minutes. For anatomic registration and normalization, high resolution, T1-weighted MPRAGE images were collected with flip angle=7º, minimum full echo time, inversion time=425ms, acquisition voxel size=1mm isotropic.

Image Processing

All images were processed using the Analysis of Functional Neuroimages (AFNI) (Cox, 1996). EPI images were processed by excising the first 4 volumes, limiting each voxel's BOLD signal to four standard deviations from the mean trend of its time series, correcting for slice timing, registering by affine transformation to AFNI's TT_N27 Taliarach template, and smoothing using a 4mm full-width at half maximum Gaussian kernel, and scaling to a mean of 100. All images were visually inspected for acquisition artifact and registration.

Processed images were then entered into a general linear model with the following parameters: a cubic detrending polynomial, a regressor for each of 6 translational and rotational motion parameters, a 2s block-GAM convolved regressor for each emotion by intensity stimulus class, and a 2s block-GAM convolved regressor for stimuli with misidentified gender. EPI volumes were censored from this GLM regression by three criteria: i) any volume with a motion shift, defined as movement exceeding Euclidean distance of 1mm from its preceding volume, ii) any volume immediately preceding such a motion shift, and iii) any volume with a large fraction (>10%) of outlying time points. No more than 15% of volumes were censored. Beta values for regressors for the three emotions at 50% intensity were used in for further analysis.

References

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Supplemental Figure 1. Histogram of accuracy on the Interpretation Bias Task for all participants (n=89). The red line is at 70% accuracy, the threshold for inclusion in analysis.

Supplemental Figure 2. The implicit emotional processing task. Task procedure and sample face emotion stimuli for the implicit emotion processing task used to elicit neural activation to subtle emotional expressions. See main text for task description